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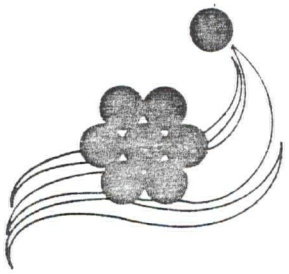
ENVIRONMENTAL IMPACT STATEMENT FOR ASARCO, INCORPORATED VARIANCE FROM PSAPCA REGULATION I SECTIONS 9.03(b), 9.07(b), AND 9.07(c)



PUGET SOUND AIR POLLUTION CONTROL AGENCY (PSAPCA)

MARCH 1981

4.10 ARSENIC HEALTH EFFECTS

4.10.1 Introduction

Arsenic exposure can occur through the air, food, water, drugs, and accidental or deliberate poisoning. Smelting of metal ores, burning of fossil fuels, and pesticide use are the main man-made sources. The greatest risk from these is through occupational exposure, but significant exposures can also arise in those who are not occupationally exposed through the dissemination of emissions, or the accumulation of arsenic residues in water supplies or on food.

Arsenic is widely distributed in animals and plants. Indeed there is evidence that it is an essential constituent of the diet in certain animals, though this has not been certainly shown to be the case in man. The chemical form of the arsenic is important. Much of the high concentration of arsenic in marine life is present in the form of complex organo-arsenical coumpounds. These are either not, or only minimally, metabolized and for the most part are rapidly excreted unchanged. Presumably they are, therefore, toxicologically inert. Trivalent compounds are generally agreed to be more toxic than pentavalent compounds, and inorganic compounds more than organic. These facts need to be kept in mind when considering total body burden of arsenic or input/output balance of the body.

4.10.2 Normal Arsenic Values

The normal human blood arsenic is variably given as under 5 µg/l (0.005 ppm) to as high as 60 µg/l (0.060 ppm) (National Research Council, Committee on Medical and Biological Effects of Environmental Pollutants 1977). On the whole, blood arsenic has not proved useful in studies of adverse health effects. Urinary arsenic, however, has been used much more often. Moderate correlations have been shown (r=0.5-0.6)* between levels of arsenic in air or water and levels in urine (Pinto et al.

*r = correlation coefficient

1977). The normal concentration is sometimes considered to be under 50 µg/l, but levels considerably higher are often reported, particularly if much seafood is consumed. Arsenic in hair is normally less than 1 ppm though again higher values are sometimes recorded.

In 1964/1965, average annual concentrations of arsenic in the ambient air at the stations included in the National Air Sampling Network (NASN) varied from 0 to 0.75 µg/m^3. The highest value of 0.75 µg/m^3 was recorded at El Paso, Texas, where the average for one quarter reached 1.40 µg/m^3, but a high concentration (average annual 0.25 µg/m^3) was also recorded in Charleston, West Virginia. These concentrations are compatible with 24-hour concentrations of arsenic of about 4 to 6 µg/m^3, though occasional levels could be appreciably higher than this. Local measurements in the vicinity of the Tacoma smelter have shown 24-hour concentrations of greater than 4 µg/m^3 for about 3 percent of all monitored values (see Section 4.2.3 and Appendix C, Table C-6). Most of the NASN average annual values were in the 0.01-0.03 µg/m^3 range.

Most water supplies in the U.S. contain less than 10 µg/l (10 ppb) though levels of up to 2 ppm have been documented for some wells. The maximum allowable concentration of arsenic in drinking water is currently 50 µg/l (50 ppb). High concentrations have been reported in Oregon, one well in Lane County having 2,150 µg/l (2,150 ppb) (Whanger et al. 1977).

Arsenic is also a constituent of tobacco. Between 1940 and 1950 figures of up to 50 to 60 ppm were reported in the dry leaf of American cigarettes (Guthrie and Bowery 1967). The most recently published range is 0.5 to 0.9 ppm (Griffin et al. 1975). Of the arsenic in cigarette tobacco 2.2 to 8.6 percent is transferred to the respiratory tract (U.S. Office on Smoking and Health 1979).

4.10.3 Daily Intake of Arsenic

The daily intake of arsenic can be calculated roughly as follows:

Air: Assuming 0.03 µg/m^3 in urban air and 20 m^3/day, the total intake would be 0.6 µg.

Water: Assuming 10 µg/l and 2 liters daily consumption, the intake from water would be 20 µg.

Food: Assuming 20 µg and 80 percent absorption intake: 16 µg.

For a nonsmoker, the total daily intake might therefore be about 36 µg. The intake from food may be very much higher than these figures suggest if much seafood is consumed. But if the arsenic in seafood is metabolically inert, this may be of little significance (although it will clearly confound estimates of exposures from other sources). Smoking will add a small amount to this total daily intake. But at most, this should not be more than about 1 µg per pack of 20 cigarettes.

A daily urinary excretion of 50 µg/l should adequately eliminate this amount of arsenic and provide a considerable margin of safety for additional daily intake.

4.10.4 Effects of Arsenic Exposure on Health

The classical descriptions of arsenic intoxication usually classify the manifestations under acute, subacute, and chronic categories. Such a classification is not helpful to our present purpose which is to assess the long-term effects of exposure to low or relatively low concentrations. In these circumstances, a more useful classification is:

I. Carcinogenic effects
   (i) skin
   (ii) respiratory
II. Noncarcinogenic skin or respiratory changes (pigmentation, keratoses, warts, perforation of the nasal septum, etc.)
III. Increased body burden, particularly raised urinary arsenic
IV. Other miscellaneous effects
   (i) suggestive symptoms, such as dyspepsia, diarrhea, paraestheias (pins and needles, numbness), weakness of the limbs, bronchitis
   (ii) changes in nerve conduction velocity
   (iii) "Blackfoot" or other peripheral vascular disease
   (iv) chromosome abnormalities

Skin cancer was first attributed to arsenic in smelter workers by Paris (1820) on evidence which was subsequently impugned (Butlin 1892, Kennaway 1942). However, it now seems clear that arsenic can contribute to the development of skin cancer (Neubauer 1947; Hill and Faning 1948; Fierz 1965; Tseng et al. 1968). Respiratory cancer has been linked to arsenic more recently and this association is still a legitimate question for debate. The well established relationship between degree of arsenic exposure and level of respiratory cancer (Lee and Fraumeni 1969; Ott et al. 1974; Pinto et al. 1978) clearly indicates that arsenic may contribute to this disease. But the respective roles of arsenic exposure and other respiratory tract irritants, notably cigarette smoking, still need to be elucidated. The evidence against the carcinogenicity of arsenic has been well summarized by Pelfrene (1976).

Skin cancer usually arises on a basis of chronic arsenicism--hyperkeratosis, warts, pigmentation, and vascular changes (Neubauer 1947; Hill and Faning 1948; Roth 1958; Tseng et al. 1968; Tseng 1977). It is frequently multiple (Neubauer 1947) and often characteristic with regard to its distribution. It is particularly likely to occur on the palms of the hands and soles of the feet where skin cancer from other causes, notably sunlight, is notoriously rare. Respiratory cancer, on the other hand, though it may occur in cases of chronic arsenicism, for example in the German vineyard workers (Roth 1958; Braun 1958), or among the Gwanda gold miners (Osburn 1957; 1969) does not usually seem to be associated with evidence of arsenic poisoning.

In this consideration of the effects on health of arsenic exposure, the emphasis will be on those studies which provide useful evidence on safe levels. No attempt will be made to review all the studies of arsenic effects; only, for the most part, those which provide some basis for drawing useful conclusions will be presented. Since the Tacoma smelter is the focus of the current impact statement, it may be best to start with a review of the evidence which has come to light over the years of potential for arsenic exposure and its effects on the employees and on the surrounding population.

The U.S. Environmental Protection Agency has designated inorganic arsenic a hazardous air pollutant under the federal Clean Air Act. The Federal Register announcement of this designation (45 Fed. Reg. 37,886 (1980)), which contains a summary of the EPA findings on arsenic health effects, is reproduced as Appendix H.

4.10.5 Evidence from the Tacoma Smelter and the Surrounding Neighborhood

In an early study, Pinto and McGill (1953) studied urinary arsenic concentrations in 348 men exposed to arsenic trioxide dust during the course of their work and in 124 individuals working in industry but having no known exposure to arsenic. The mean concentration of 835 spot samples of urine from the exposed workers was 0.82 mg/l (median 0.58 mg/l) compared with 0.13 mg/l (median 0.10 mg/l) for the 147 spot samples from the nonexposed. About 12 percent of the nonexposed had values gerater than 0.3 mg/l. Interpretation of such values is difficult. They may reflect exposure to arsenic in the ambient air or at work, but they may also reflect ingestion of arsenic in the diet.

Acute arsenical dermatitis was a common occurrence in the employees of the smelter in the early 1950s. Pinto and McGill found that its frequency increased progressively from a background value of about 30 percent in those persons with a urinary arsenic concentration of 0.3 mg/l to 100 percent in those with a urinary arsenic concentration of 3.0 mg/l or more. Presumably these urinary arsenic concentrations reflect air arsenic concentrations, which are sufficiently high to provide skin sensitivity. Certainly the red, inflamed, weeping eczema, described by Pinto and McGill (1953) and Holmqvist (1951) is quite different from the pigmented skin lesions of chronic arsenicism. The evidence presented by Pinto and McGill (1953) suggests that it is desirable to avoid urinary arsenic levels of 0.3 mg/l or more. Some 15 years later, it was shown (Pinto et al. 1977) that a urinary concentration of 0.3 mg/l is roughly equivalent to an airborne exposure of about 0.09 mg/m^3. This suggests that the then current time weighted average (TWA) occupational standard for arsenic of 0.5 mg/m^3 was too high and provides some evidence, on the basis of acute irritant dermatitis, that 100 $\mu g/m^3$ might be a more acceptable level.

Pinto and Bennett (1963) compared the number of deaths from various causes which ocurred from 1946 to 1960 in the smelter workers with the number which would have been expected if the State of Washington's proportional rates for 1958 had applied to the smelter population. The number of deaths from all cancer and from respiratory cancer among smelter wokers was greater than would have been expected for the State of Washington. Thus, 35.8 deaths from all cancer were expected, whereas 43 were observed; 8.6 cases of cancer of the lung were expected, whereas 18 were observed--an appreciable excess. However, the excess of cancer appeared to be no different in those exposed to arsenic than in those not exposed. The authors concluded that exposure to arsenic trioxide of the amount described has no effect on cancer or fatal cardiovascular disease. Despite the authors' claim that the question of arsenic exposure or nonexposure was clear cut and based on a firm foundation, it is difficult to accept the validity of their exposure dichotomy, particularly since this was carried out after death. There is also a possibility that bias could have been introduced into the results by basing the expected deaths on 1958 when the collection period in the smelter ran from 1946 to 1960. Results which are based on the use of proportional mortality rates should also be treated with caution.

Milham and Strong (1974) reviewed deaths from 1950-1971 among residents of Pierce County, Washington, the county in which the Tacoma smelter is situated. They identified 39 deaths due to respiratory cancer among persons who listed employment in the smelter. On the basis of U.S. rates, 18 deaths would have been expected. Thus, an increased mortality rate from respiratory cancer among the smelter workers was confirmed.

Milham and Strong also compared arsenic in urine and arsenic in hair among children attending two schools, one within 300 yards from the stack of the smelter, the other (a control), 8 miles away. Significantly higher levels were observed in the school children attending the school near the smelter. All but one of the children in the control school had arsenic levels of less than 60 µg/l (0.06 ppm). Most of the children in the school near the smelter had urinary arsenic concentrations of 60 µg/l or more. Arsenic in hair was also high in these children. A good

relationship was shown between the urinary arsenic concentrations and the distance of residence from the smelter. The mean urinary arsenic of persons living within 2 miles of the smelter was 60 µg/l (0.06 ppm) or over. While this may suggest that at this time, air arsenic concentrations were undesirably high, it may also reflect the accumulation in soil or house dust of past air arsenic levels, which were higher. The implication of these urinary concentrations is uncertain. Milham failed to show any differences between exposed and nonexposed children in auditory acuity, blood status, or school attendance despite these elevated urinary arsenic levels (Milham 1977). No information is, however, available on the long-term implications, particularly in relation to experience of cancer.

The most useful studies of employees in the Tacoma smelter for our present purpose are those of Pinto et al. (1977; 1978). These investigators studied the mortality of all pensioners aged 65 and over from 1949 to 1973. The overall mortality of the cohort was 12.2 percent higher than for males living in the same area, of the same ages and same time periods. The excess mortality was chiefly due to respiratory cancer where mortality was three times that expected. From urinary arsenic levels in 1973, an arsenic index was developed for each operation in the plant. Urinary arsenic concentrations had been shown to correlate fairly well ($r=0.53$) with airborne arsenic concentrations obtained by personal monitoring. The regression of airborne arsenic concentration (y) on the urinary arsenic concentration (x) was $y = 0.304\ x$. On the basis of occupational histories, a working lifetime exposure was estimated for each man. Observed and expected deaths from respiratory cancer were related to this index (Table 4.10-1). There was a clear dose/response reationship between respiratory cancer mortality and estimated lifetime arsenic exposure. The risk increased from no difference from expectation in the lowest exposure category to eight-fold higher in the highest. Since pollutants other than arsenic were present in the air, the authors were cautious in claiming the carcinogenicity as due to arsenic. However, the close association with arsenic dosage provides persuasive evidence for this conclusion.

TABLE 4.10-1

OBSERVED AND EXPECTED RESPIRATORY CANCER DEATHS AND STANDARDIZED MORTALITY RATIOS BY ARSENIC EXPOSURE INDEX FOR TACOMA SMELTER EMPLOYEES

			Respiratory Cancer Deaths		
Exposure Index	Mean Index	Number of Men	Observed	Expected	Standardized Mortality Ratio
Under 2,000	1,514	36	1	0.9	111.1
2,000-2,999	2,513	109	4	2.1	190.5
3,000-5,999	4,317	205	11	3.9	282.0(a)
6,000-8,999	7,473	109	7	2.3	304.3(a)
9,000-11,999	10,135	38	4	0.7	571.4(a)
12,000 and Over	14,712	29	5	0.6	833.3(a)

Data from: Pinto et al. 1977; 1978.
(a) Significance level of $P<0.05$

4.10.6 Evidence from Other United States Smelters

The mortality of 8,047 smelter workers in the Anaconda smelter in Anaconda, Montana was studied by Lee and Fraumeni (1969). All men who had worked for at least 12 months during 1938 to 1956 were followed. Mortality to 1963 was compared with expectations based on the State of Montana using the standard life table method. Overall there was a three-fold excess of respiratory cancer among the smelter workers. This, however, rose to eight-fold in the most heavily exposed workers with the longest latency since first exposure. Total mortality was also increased with excess deaths from tuberculosis, heart diseases, and cirrhosis of the liver. In this study, arsenic exposure was based on estimates of maximal arsenic exposure. In a further study of the employees in this smelter, the possibility of deriving better lifetime estimates of exposure was explored in a small pilot random sample (Higgins et al., unpublished). Preliminary estimates suggest that very high death rates occurred with very high arsenic doses (Table 4.10-2). In the "light" arsenic exposure group, still excessive by current thinking but below the American Conference of Governmental Industrial Hygienists (ACGIH) TWA of 500 $\mu g/m^3$, the Standardized Mortality Ratio* (SMR) for lung cancer (based on the very

*SMR computed as (observed deaths ÷ expected deaths) x 100.

TABLE 4.10-2

MORTALITY FOR REVISED EXPOSURE CATEGORIES
ALL 300 MEN IN THE SAMPLE
ANACONDA SMELTER EMPLOYEES

	Arsenic Concentration								
	High ≥10.0 mg As/m^3			Medium 0.5-10.0 mg As/m^3			Low <0.5 mg As/m^3		
Number in Sample	28			135			137		
Deaths:	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
All Causes	20	7.93	252(a)	77	57.17	135(b)	60	48.44	124
Lung Cancer	6	0.42	1429(a)	5	2.56	195	3	1.77	170

Data from: Higgins et al. unpublished.
(a) Significance level of P<0.01
(b) Significance level of P<0.05
OBS = observed
EXP = expected
SMR = Standardized Mortality Ratio

small numbers) was 170. The study is continuing with the intention of categorizing the workers exposed to 500 µg/m^3 and less to see if there is a threshold dose which might be considered safe. An attempt was also made in this study to obtain smoking habits retrospectively from all members of the sample to see if arsenic exposure was confounded with cigarette smoking. While those most heavily exposed to arsenic tended to be somewhat heavier smokers, cigarette smoking cannot explain the increased risk due to arsenic exposure.

Rencher et al. (1977) and Rencher et al. (1979) studied employees at the Kennecott Copper Corporation's smelter near Salt Lake City, Utah. In an analysis of deaths of current and former employees during the 11 years, 1959 to 1969, they found that the death rates for lung cancer among smelter workers were higher than those for employees in the mine and concentrator and also than those for all males in the State of Utah. Lung cancer mortality was associated with a high index of exposure to arsenic, SO_2, H_2SO_4, lead, and copper. Unfortunately, from the data

presented in the report, it is not possible to form any idea of the arsenic concentrations to which these smelter workers might have been exposed before 1959. Most of the lung cancer deaths occurred in workers who had been employed before this year.

On the basis of indemnity insurance claims, these research workers also studied morbidity. They found that the refinery rather than the smelter was the source of the largest number of claims.

4.10.7 Evidence from Smelters Outside the U.S.

Studies have been conducted in and around smelters in Sweden. A smelter began operations in 1928 in Ronnskar. It produces copper, lead, gold, silver, zinc clinker, arsenic trioxide, arsenic, selenium and selenium compounds, and nickel sulfate. Arsenic, lead, cadmium, mercury, SO_2, and sulfuric acid are emitted. Two years after the start of operations eczematous skin lesions began to occur among the employees (Holmqvist 1951). The average sick leave for the initial illness was 13.6 days and for each recurrence a further 10.2 days. Between 1932 and 1948, the conditions in the plant improved with resultant improvement in the frequency of occurrence of eczema from 219 cases in 1932 to 12 cases in 1948. It was thought at first that the eczema was caused by sulfuric acid in the crude arsenic powder. Careful patch testing, however, indicated that arsenic and not sulfuric acid was responsible.

Holmqvist (1964) found that the pattern of mortality in the plant from 1940 to 1960 was similar to that expected for the total population of Sweden except for an increase in lung cancer among the smelter workers. This could not, however, be definitely linked with arsenic trioxide exposure.

Axelson et al. (1978) also studied mortality in the Ronnskar smelter using the register of parish deaths and burials. Among men aged 30-74, 369 deaths were recorded during 1960-1976. Men who died from lung cancer, cardiovascular disease, haemolymphatic malignancy, and cirrhosis of the liver were compared with men who died from all other causes of death.

Lung cancer was increased five-fold and cardiovascular disease about two-fold and there was a dose-response relationship with arsenic exposure. The concentration of arsenic was based on estimates for the different departments from 1928. Three exposure levels around 0.5 mg/m^3 were used with the lowest considerably below 0.5 mg/m^3, the second close to but not exceeding 0.5 mg/m^3, and the third over 0.5 mg/m^3. It is not clear what measurements were actually made, nor how changes in arsenic concentrations over the years were allowed for. Indeed it is not clear if any arsenic measurements were used. The study provides support for the belief that arsenic exposure contributes to lung cancer and to cardiovascular disease. It may also provide support for the view that exposures to 0.5 mg/m^3 are too high. But it does not help very much in estimating what maximal concentration might be permissible.

4.10.8 Health of Persons Living in the Vicinity of Smelters

It has been estimated that from 1930 to 1960 the Ronnskar smelter emitted 1-3 tons of arsenic daily into the ambient air. Persons who lived in the vicinity of the smelter were studied by Pershagen et al. (1977). These research workers studied mortality of the residents of two parishes in the direction of the prevailing wind from the smelter. They compared the death rates with a reference population similar in degree of urbanization, occupational profile, and fraction of the population working, situated 200 kilometers to the south and presumably, therefore, free from arsenic pollution. A significant excess of lung cancer was observed in men but not in women. When occupation was considered, most of the male excess could be explained by occupational exposure within the smelter. Unfortunately, no measurements of ambient air concentrations were presented. Consequently, it is impossible to draw quantitative conclusions. However, it seems likely that these ambient air concentrations must have been high. Within the plant, lung cancer apparently occurred in excess frequency. No such excess occurred in the down-wind and presumably heavily polluted neighborhoods. Clearly a latency of 50 years is adequate for any such risk to have become apparent.

Mortality from respiratory cancer and other diseases has long been known to be high in three counties (Deer Lodge, Silver Bow, and Lake) in Montana (Hueper 1955). In 1947/1948 it was observed that the respiratory cancer rate in these counties was 46.3 to 145.7 per 100,000 whereas in an agricultural county in Montana the rate was 5.2 per 100,000. At that time the average U.S. rate was 10.9 per 100,000. The hypothesis was advanced that these high rates might be due to arsenic emissions from mining and smelting operations. This hypothesis is hard to test now in any rigorous way. Some of the excess deaths are due to the fact that the inhabitants of these three Montana counties were older than the average for Montana or the United States. Some of the excess must certainly have been due to occupational exposures. Radioactivity of building materials has been suggested more recently as a possible cause of respiratory and other cancer. Differential migration of younger, fitter persons from these areas may also have played a part in the high rates quoted by Hueper. These factors cannot now be satisfactorily disentangled.

An excess of lung cancer for white males in counties refining and smelting nonferrous metals was suggested by Blot and Fraumeni (1975). The authors attributed the excess to arsenic. There were, however, a number of problems. No measurements of arsenic were made. Refining and smelting counties were not considered separately (Nelson 1977). More important, however, is the fact that lung cancer mortality varies approximately two-fold over the various states. It appears wrong to compare smelting and refining counties with all United States counties. Rather the comparison should have been of smelting and refining counties and nonsmelting and refining counties within individual states. When this is done (see Table 4.10-3) the excess noted by Blot and Fraumeni disappears.

4.10.9 Manufacture of Arsenicals

Ott and his colleagues (Ott et al. 1974) studied workers exposed to arsenic in the manufacture and packing of insecticides from 1919 through 1956. Between 1940 and 1972, 2,000 employees were known to have died. Employee histories of these men were scrutinized to identify any man who

TABLE 4.10-3

COMPARISON OF LUNG CANCER RATES BETWEEN
COPPER SMELTING COUNTIES AND THE TOTAL STATE, 1950-1969

County			State		
	White Males	White Females		White Males	White Females
Deer Lodge	65.2	4.2	Montana	31.10	4.77
Gila	46.3	7.3	Arizona	39.51	6.41
Pima	39.7	6.7	Arizona	39.51	6.41
Cochise	38.1	6.0	Arizona	39.51	6.41
Pierce	35.8	6.4	Washington	34.61	6.12
El Paso	33.9	7.6	Texas	38.52	6.55
Greenlee	32.0	2.1	Arizona	39.51	6.41
Pinal	31.7	7.8	Arizona	39.51	6.41
Ontonagon	29.2	2.0	Michigan	39.09	5.95
Polk	28.8	4.4	Tennessee	33.48	5.45
Grant	26.3	10.8	New Mexico	24.71	6.26
Salt Lake City	26.2	3.5	Utah	21.98	3.26
White Pine	20.0	5.8	Nevada	41.85	7.96
Average	34.9	5.7		35.6	6.03
National Average	38.0	6.3			

Data from: Mason and McKay 1974.

had spent 1 or more days in the production unit. The exposed population consisted of 173 men; the rest of the decedents served as controls. Proportional mortality rates in exposed workers and controls were compared. Cancer of the respiratory system was 3 times as frequent among the exposed group as among the controls (16.2 percent compared with 5.6 percent). On the basis of available environmental measurements and different job classifications, an estimate was made of the cumulative lifetime exposure of each employee. A dose-response curve was derived which showed that the risk of respiratory cancer increased from roughly expectation in the lowest to 6 times expectation in the highest exposure group (Table 4.10-4).

Ott and his colleagues then followed a group of 603 men who had worked in the production area, who had not been exposed to asbestos (a known carcinogen) and who were still employed by the company in 1940 to assess their mortality experience. Mortality rates for white males in

TABLE 4.10-4

RESPIRATORY CANCER DEATHS BY EXPOSURE CATEGORY
IN ARSENICAL INSECTICIDE EMPLOYEES

Average ln Dosage (in mg Arsenic)	Projected 8-hour TWA(a) (ug Arsenic)	Total Deaths (n = 173)	Respiratory Cancer Deaths		
			Observed (n = 28)	Expected	O/E(b)
3.74	1.0	26	1	1.77	0.6
4.84	3.0	17	2	1.01	2.0
5.53	6.0	24	4	1.38	2.9
6.04	10.0	22	3	1.36	2.2
6.68	20.0	27	3	1.70	1.8
7.35	40.0	18	2	0.97	2.1
8.17	90.0	13	3	0.77	3.9
8.78	160.0	13	5	0.79	6.3
10.30	740.0	13	5	0.72	7.0

Derived from: Ott et al. 1974; Blejer and Wagner 1976.
(a) Time Weighted Average
(b) observed ÷ expected
Note: ln = natural logarithmic

the United States formed the basis for comparison. A three-fold excess of respiratory cancer and an approximately four-fold excess for lymphatic and haematopoietic tissue malignancies were found.

Mabuchi and his colleagues (1979) studied workers exposed to arsenic during manufacturing and packaging of pesticides in a plant in Baltimore, Maryland. A follow-up of workers employed during the period 1946-1974 was carried out. Since difficulties were anticipated in tracing temporary, short-term employees, a 20-percent sample of the 2,189 workers with less than 4 months employment were selected. In all, 1,393 persons (1,050 males and 343 females) were followed. The expected number of deaths was based on the white rates for the City of Baltimore. The standard life table method was used to cumulate person-years of observation for 5-year age groups and 5-year calendar periods. The standardized mortality ratio for lung cancer for men was moderately raised (168) but not for women. Exceptionally high mortality was also attributed among men to the anaemias. Unfortunately, only crude and nonquantitative estimates of exposure were available. For lung cancer there was an increasing gradient in Standardized Mortality Ratio with increasing duration of exposure to arsenicals. This

was interpreted by the authors to indicate a probable dose-response relationship. For our present purpose, little use can be made of these data.

4.10.10 Arsenic Contamination of Drinking Water

Arsenic poisoning has long been known to occur in Cordoba Province in the Argentine (Ayerza 1918), and in Reichenstein in Silesia (Kathe 1937). In 1962 the first cases of children with cutaneous lesions of chronic arsenic poisoning were detected in Antofagasta, Chile (Zaldivar 1974). Contamination of the town's drinking water from the Toconce River apparently occurred over a number of years. Concentrations of 600 to 800 µg As/l were observed. Arsenical pigmentation associated with hyperkeratosis, chronic cough and bronchopulmonary disease, cardiovascular manifestations, such as Raynaud's syndrome, acrocyanosis, angina pectoris and hypertension, abdominal pain and diarrhea were described. The arsenic content of urine, hair, and nail clippings was found to be high, 0.42 mg/100 g, compared with that found in an arsenic-free community.

Table 4.10-5 shows the arsenic concentration and rates of chronic arsenical poisoning for the years for which these are available. In 1970 a filtration plant was installed with immediately beneficial effect. Zaldivar (1974) quotes maximum acceptable concentration values of arsenic in drinking water for various countries:

World Health Organization (1958 and 1961)	0.20 ppm	200 µg/l
Great Britain	0.20 ppm	200 µg/l
Argentina	0.12 ppm	120 µg/l
Chile	0.12 ppm	120 µg/l
U.S. Public Health Service	0.05 ppm	(50 µg/l)
but recommending	0.01 ppm	(10 µg/l)

In Taiwan, artesian well water with a high arsenic content has been used for more than 60 years. A high prevalence of endemic arsenicism has been observed more recently (Yeh 1963, Tseng et al. 1968). The arsenic concentration in the drinking water ranged from 0.01 to 0.82 ppm.

TABLE 4.10-5

ARSENIC CONCENTRATION IN DRINKING WATER (ppm)
AND MEAN ANNUAL INCIDENCE OF CHRONIC ARSENIC POISONING
IN ANTOFAGASTA, CHILE

Year	Number of Cases	Arsenic Concentrations		Incidence/100,000/year	
		Mean	Range	Male	Female
1955	80	0.44	0.05-0.92		
1961	183	0.66	0.11-0.90		
1967	28	0.63	0.45-0.80		
1968	49	0.63	0.25-0.90	87.9	99.5
1969	231	0.56	0.13-0.96	203.5	236.6
1970	42	0.78	0.66-0.82		
1955-70		0.5980	0.05-0.96		
1970	56	0.08	0.05-0.18	19.8	21.6
1971	178	0.08	0.02-0.40	9.1	10.0
1972	19	0.10	0.04-0.25		
1970-72		0.0815	0.02-0.40		

Data from: Zaldivar 1974.

Hyperpigmentation, keratosis, skin cancer, and peripheral vascular disease, notably "blackfoot disease," so called because of the resultant gangrene of the extremities, were seen. All were related to the dosage of arsenic obtained from the drinking water, rising from a low prevalence at concentrations of under 0.3 ppm to a high at concentrations of 0.6 ppm and over. Unfortunately, insufficient information has been presented for estimating risk at different concentrations below 0.3 ppm. We can only conclude that permissible concentrations of arsenic in drinking water should be less than 0.3 ppm (300 µg/l).

The highest concentrations of arsenic in drinking water in the United States occur in Lane County, Oregon. Concentrations up to 2 parts per million in one well have been recorded (Whanger et al. 1977). These high arsenic concentrations are due to the underlying geological system of sedimentary and volcanic rocks known as the Fischer formation. Despite high concentrations, there is little evidence of arsenic toxicity. A few cases with mild, if slightly suggestive, symptoms of arsenicism have been described. Morton et al. (1976) studied skin cancer morbidity

from 1968 to 1974. No relationship between arsenic concentrations and the occurrence of skin cancer could be demonstrated. This may be because the arsenic levels in general were too low. Only 5 percent of the water samples tested during the survey showed concentrations of 100 ppb or over. Other studies of moderately elevated levels of arsenic in drinking water have reached broadly similar conclusions (Harrington et al. 1978; Goldsmith et al. 1972).

4.10.11 Agricultural Exposures to Arsenicals

Most of the exposures to arsenic encountered in the German vineyard workers (Roth 1957; Braun 1958; and Butzengeiger 1940) appear to have been to high (and usually unspecified) concentrations. No conclusions can be drawn from them about safe exposure levels.

The study of mortality among the orchard workers exposed to lead arsenic spray conducted by the U.S. Public Health Service (Nelson et al. 1973), which at first sight might provide information on safe exposures, is unfortunately of questionable validity. Other evidence suggests that mortality may have been seriously underestimated (Milham 1974; National Institute for Occupational Safety and Health 1975). In the circumstances, no use can be made of the quantitative exposure information presented.

4.10.12 Formulation of a Safe Arsenic Intake

From Pinto et al. (1977) we might infer that the lowest index of exposure in their table could form a basis for a safe working level, namely a mean index of 1,514. Assuming a working lifetime of 25 years, this index points to an upper urinary arsenic of $1,514 \div 25 = 60.6$ µg/l. Assuming a regression of y (air arsenic) = 0.304x (urinary arsenic) (see Section 4.10.5), 60.6 µg/l in urine is equivalent to 18.4 $\mu g/m^3$ air exposure. Air arsenic levels in the smelter have declined greatly during the lifetime of the pensioners studied. They were 20 or more times higher in the past. Urinary arsenic values have declined about two-fold over the same time. A conservative estimate of air values during a man's working lifetime might therefore by twice the 18.4 $\mu g/m^3$ measured in

1973, while even a five-fold reduction might be reasonable. Doubling 18.4 gives us 36.8 $\mu g/m^3$, while multiplying by 5 gives 92.0 $\mu g/m^3$. It would appear that the standard originally suggested by NIOSH (1973) of 50 $\mu g/m^3$ for a TWA would be reasonable.

An occupational standard can be translated to an ambient 24-hour standard by dividing by a factor of 12 (roughly 4 times for the number of working (40) to total (168) hours per week and 3 times for the working as a proportion of the total lifetime (25 to 75 years.) Thus, an ambient concentration of 1 to 3 $\mu g/m^3$ day-in, day-out could probably be safely dealt with (by the healthy normal subject). Such a standard, however, does not allow for the possibility that there might be persons in the general population who may be unduly susceptible to arsenic, who are not represented in an occupationally exposed group. This criticism is often raised when extrapolation from an occupational population to the general community is attempted. Examples to support its validity in the area of cancer are hard to find.

The second study which one would like to be able to use to derive a safe level of arsenic exposure is that of Ott and his colleagues (Ott et al. 1974). Again, a dose-response relationship between arsenic exposure and respiratory cancer risk was shown, but here on the basis of comparisons only of those who died. As in the study by Pinto et al. (1977) no excess risk was seen in the lowest exposure category (less than 1 mg As/m^3-months). The response was flat at about twice the expected risk up to 10 mg As/m^3-months. If we apply the same assumptions to the Ott study that we applied to the Pinto study, we might conclude that over a working lifetime of 25 years, one should not be exposed to more than 1,000 ÷ 25 = 40 μg As/m^3-months or 3-1/3 μg As/m^3-years. We might have reservations about the lower end of the dose-response curve and wonder if up to 10 times this concentration might not be acceptable. This would lead us to a critical concentration of arsenic in the work place very similar to that reached from considering the Pinto study.

There are serious reservations from using the Ott study in this way. As already mentioned, risk was based on a retrospective study of the

deaths. One has to assume that exposures of those who died were representative of those members of the cohort from which the deaths came. This may or may not be so. The evidence has not been presented which would allow one to judge. The curiously flat part of the dose-response curve from 1 mg to 10 mg As/m^3-months has also been noted. This raises the possibility of other factors and particularly other exposures influencing the relationship. In fact, such other exposures were numerous and varied even at the plant studied by Ott. Two of the workers who died had been exposed to asbestos, a known respiratory carcinogen, and there were also exposures to benzene, ethylene dibromide, and many other chemicals.

Many of the exposures in the arsenic production unit were to high concentrations for a short time. The "concentration times years" approach to dosage does not differentiate short high dosages from longer exposures to lower concentrations. This must inevitably raise doubts about the validity of the procedure for our present needs.

No allowance was made for smoking, which could also have been important, especially when estimates depend on such small numbers of persons in the different dosage categories.

The third study which provides a pointer toward safe arsenic concentrations is that of Perry and his colleagues (Perry et al. 1948) in the sheep dip factory where excess cancer mortality had been observed by Hill and Faning (1948). Hill and Faning had noted that all the lung and skin cancer deaths (5 and 3, respectively) had occurred among the chemical workers in the factory. Perry and his colleagues carried out clinical and environmental investigations in the plant. They showed that the median concentrations of arsenic to which the workers were exposed were 0.254, 0.373, and 0.696 mg/m^3 in the drying room, sieving room, and near the kibbler operator, respectively. Arsenic levels in the packing room were much lower, 0.071 mg As/m^3. Their chemical observations are summarized in Table 4.10-6. Urinary arsenic concentrations were not very different in the maintenance workers or packers than in the unexposed workers. Hair concentrations were moderately increased more in the maintenance workers than in the packers. Pigmentation was slightly

TABLE 4.10-6

MEASUREMENTS OF ARSENIC AND CLINICAL SIGNS AMONG SHEEP DIP WORKERS

Category	Number	Urinary Arsenic (mg/l)	Hair (ppm)	Number with Warts	Clinical Pigmentation[a] (percent)					
					0	+	++	+++	++++	Total
Chemical	31	0.24	108	29	10	32	29	23	6	100
Maintenance	20	0.10	85	3	63	28	9	0	0	100
Packers	12	0.11	64							
Unexposed	56	0.09	13	4	82	14	4	0	0	100

Data from: Perry et al. 1948.
(a) the scale from 0 to ++++ represents increasing clinical levels of pigmentation.

increased, but warts no different in packers and maintenance workers than among controls. Thus, one might conclude from these observations that a median air arsenic of 71 $\mu g/m^3$ should not present much of a hazard.

4.10.13 Various Recommendations Which Have Been Made for an Arsenic Standard (Workplace)

In 1943 the American Standards Association (now the American National Standards Institute [ANSI]) recommended 0.015 mg As/m^3 as the American war standard for inorganic arsenic. However, by 1956 the war standard had been increased to 0.15 mg As/m^3, a ten-fold increase, based on analogy with such metals as cadmium and lead. This concentration was adopted by Connecticut, Massachusetts, New York, and Oregon. Utah endorsed a maximum acceptable concentration (MAC) of 0.5 mg/m^3.

In 1947 the American Conference of Governmental Industrial Hygienists (ACGIH) adopted a MAC for arsenic of 0.1 mg/m^3, but the following year raised it to 0.5 mg As/m^3. No explanation was given for this change. Pinto, however, stated that a "safe concentration was interpreted as one that 'would not cause incapacitating dermatitis in a few hours'". There is uncertainty whether the 0.1 mg/m^3 was a ceiling value and the 0.5 mg/m^3 a TWA. But if so, the change would constitute a 15-fold increase.

In 1959, Elkins recommended a MAC of 0.25 mg/m^3 for arsenic trioxide, equivalent to 0.18 mg/m^3 of arsenic. Watrous and McCaughey's (1945) report of concentrations averaging 0.2 mg As/m^3 in the manufacturing department of a pharmaceutical plant appears to have formed the basis for this recommendation.

The ACGIH has recommended separate threshold limit values (TLVs) for lead arsenate and calcium arsenic for years. A limit of 0.15 mg/m^3 for lead arsenate, equivalent to 0.026 mg/m^3 of arsenic was adopted in 1956, confirmed in 1957, and has remained unchanged ever since. A limit of 0.1 mg/m^3 for calcium arsenate (equivalent to 0.038 mg As/m^3) was recommended by the ACGIH in 1956 and adopted in 1957. In reviewing the standards, Smyth (1956) attributed the toxicity of calcium arsenate to its arsenic content. Considering it to be 20 percent arsenic, he recommended a standard of 2.5 mg/m^3 to be consistent with the ACGIH's recommended standard of 0.5 mg As/m^3 for "arsenic and compounds." The ACGIH cited Smyth as attributing toxicity of calcium arsenate to the arsenic content, but the TLV recommended was 1.0 mg/m^3 equivalent to 0.38 mg As/m^3. The discrepancies are not clear.

The Czechoslovak MAC Committee suggested a mean MAC of 0.3 and a peak of 0.5 mg As/m^3. The basis for this recommendation was not given. The following MACs in other countries were noted, however: Great Britain, the United States, West Germany, and Yugoslavia: 0.5 mg As/m^3; East Germany, Hungary, and the USSR: 0.3 mg As/m^3; and Poland: 0.15 mg As/m^3. It was not stated if these MACs were ceilings or TWAs.

At the time of the NIOSH review (1973), the federal standard for "arsenic and compounds" was 0.5 mg As/m^3 as a TWA. The standards for calcium arsenate and lead arsenate were 1.0 mg $Ca_3(AsO_4)_2/m^3$ and 0.15 mg $Pb_3(AsO_4)_2/m^3$, respectively.

On the basis of the study by Perry et al. (1948) in the sheep dip workers, an average of 0.502 mg As/m^3 for all except 6 samples in the packing room is cited. From Lee and Fraumeni (1969) excess cancer in the "light" exposure area is noted after 1 to 4 years of employment. The

mean value is said to have been 0.206 mg/m^3 and the median 0.01 mg/m^3. This clearly would form no basis for any judgment of a safe level. The pharmaceutical plant study suggests a mean concentration of 0.02 mg As_2O_3/m^3 but whether this led to cancer or not is not clear.

The initial NIOSH criteria document (1973) for arsenic recommended a standard of 50 µg As/m^3 as a TWA exposure for up to a 10-hour work day, 40-hour work week. This appears to be a reasonable assessment based on the scanty evidence available. Subsequently, this figure was reduced to 2 µg/m^3 for reasons which are not entirely clear. It is likely that the major influence which led to the change was the evaluation of the study made by Blejer and Wagner (1976) of the study by Ott et al. (1974). (See projected 8-hour TWA (µg As) added to Ott's table in Table 4.10-4.) It is questionable if this study can provide reliable data in this way for the reasons which have already been given. The U.S. Occupational Safety and Health Administration has adopted a TWA of 10 µg/m^3, which on the basis of the evidence now available may be unduly stringent.

4.10.14 Conclusions

The evidence suggests that there should not be much of a hazard from a 50 µg As/m^3 TWA in the workplace or an average annual concentration of arsenic of 1 or 2 µg/m^3 in the ambient air. But we badly need more information in the workplace on the long-term effects of exposures below 500 µg/m^3. Persons living in the vicinity of smelters should also be carefully monitored, particularly those in whom urinary arsenic levels are increased.

Arsenic has been declared a hazardous air pollutant by EPA under the federal Clean Air Act (see Appendix H). This designation could lead to additional emission control requirements at the Tacoma smelter. In considering substances identified as carcinogens, EPA has adopted a no-threshold position; that is, a position that any non-zero exposure includes some risk. This EPA position is discussed in proposed rules on a "Policy and Procedures for Identifying, Assessing, and Regulating Airborne Substances Posing a Risk of Cancer" (44 Fed. Reg. 58,642 (1979)).